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Commentary

The Preventive Effect of Dietary Antioxidants on Viral Infection (Coronavirus Disease-2019, Influenza and Human Papillomavirus) and the Development of Cervical Carcinogenesis

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Viral infections cause the production of radicals and reactive oxygen species (ROS) in cells. Disbalance between ROS generation and elimination results in oxidative stress. Oxidative stress plays an important role in pathogenesis.[1] Thus, oxidative processes cause virus replication in infected cells, decrease cell proliferation and induce cell apoptosis,[2] leading to chain reactions and subsequently damaging the cells of organisms.[3] In contrast, an antioxidant is any substance that significantly inhibits or delays the oxidation of a substance.[4] The role of antioxidants is also to complete chain reactions and prevent the damage of cellular components due to free radicals and associated chemical reactions.[3,4] Beck also insisted that the antioxidant selenoenzyme, glutathione peroxidase-1, was found to be critically important, as glutathione peroxidase knockout mice developed myocarditis, when infected with a benign strain of myocarditis.[5] This work points to the importance of host nutrition in not only optimizing the host immune response, but also preventing viral mutations that could increase viral pathogenesis.

Coronaviruses (CoVs) are single-stranded ribonucleic acid (RNA) viruses which cause respiratory, gastrointestinal, hepatic and neurologic disease.[6] Above all, coronavirus disease-2019 (COVID-19) disease began to spread from Wuhan, China, in December 2019.[7,8] On March 11, 2020, the World Health Organization (WHO) announced the world wide COVID-19 pandemic only 2-months after the official disclosure from the Chinese government. Oxidative stress and lipid oxidation are involved in the pathogenesis of COVID-19-related pulmonary damage.[9]

Curcumin, a polyphenol (one of antioxidants), has been shown to target multiple signaling molecules while also demonstrating activity at the cellular level, which has helped to support its multiple health benefits.[10] Moreover, curcumin has been reported to bind to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2); the virus that causes COVID-19 target receptor.[11] Curcumin could therefore be a potential treatment option for patients with COVID-19.[12] In addition, it has been reported that the combination of vitamin C, curcumin and glycyrrhizic acid, promotes the production of interferons and regulates the inflammatory response, suggesting that the combination of these compounds may be useful in modulating the immune response to counteract the SARS-CoV-2 infections.[13] Vitamin D induces cathelicidins and defensins which can lower viral replication rates and reduce concentrations of pro-inflammatory cytokines, which produce the inflammation that injures the lining of the lungs, leading to pneumonia, as well as increase the concentrations of anti-inflammatory cytokines can also reduce risk of infection.[14] Therefore, vitamin D can reduce risk of viral infection. Grant et al[14] suggested that vitamin D supplementation may decrease the risk of contracting influenza and COVID-19 infections. In a nutritional protocol for COVID-19 patients, the supplementation of 25-hydroxyvitamin D (25(OH)D) is planned.[15]

De Alencar et al[16] reported a double-blind, randomized, placebo-controlled trial with N-acetylcysteine (NAC) as an antioxidant for the treatment of severe acute respiratory syndrome caused by COVID-19. However, no difference was observed in secondary endpoints between 67 patients in the placebo group and

68 patients in the NAC group. Thus, the administration of NAC in high doses did not affect the evolution of severe COVID-19.

It has been reported that influenza virus (IV) infection also leads to the induction of oxidative stress or ROS damage and the development of the clinical outcome.[17] Mouse models and cell lines infected with IVs showed the enhanced ROS levels, together with an imbalance of antioxidant protection.[18,19] These models indicated the relevance of the redox homeostasis induced by IVs.[20] During IV infection, the cellular metabolism of the host cells could be affected, leading to the dysregulation of redox homeostasis. Antioxidant therapies have been proposed to decrease the viral load and counteract the lung injuries caused by the overproduction of ROS induced by viruses.[21] Some antioxidants are effective in this protection against infection through the nuclear erythroid 2-related factor 2 (NrF2) pathway.[22] However, the direct clinical use of antioxidation drugs for IV-infected patients has never been reported.

Persistent infection by high-risk human papillomavirus ([HPV] types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68) genotypes has been recognized as a necessary step in the development, maintenance, and progression of cervical intraepithelial neoplasia (CIN) and cervical cancer.[23]

HPV is a small, non-enveloped deoxyribonucleic acid (DNA) virus that infects the skin or vaginal mucosal cells.[24] The circular, double-stranded viral genome is approximately 8-kb in length.

During recent decades, the important role of antioxidants in preventing the development of cervical carcinogenesis has been received much attention.[25,26] Antioxidants can act as efficient scavengers of free radicals and oxidants to prevent free-radical damage to DNA.[27] Moreover, if free radicals and oxidants are not neutralized by antioxidant molecules, the inflammatory processes caused by HPV infection could lead to extensive damage to DNA proteins.[28] The major product of DNA oxidation is also correlated with increased HPV infection, viral-host integration, and the development of dysplasia.[29] Thus, apoptosis is hindered by the disruption of many regulator pathways, which results in altered cellular proliferation.[30]

Different antioxidants may have differing abilities to intervene in the natural history of cervical diseases associated with HPV infection. The intake of caroteroids may inhibit early events of cervical cancer development (HPV infection).[31,32] The intake of vitamin A and D may also inhibit early events (from HPV infection to the development of CIN 1).[33-36] The intake of folate was reported to potentially inhibit the events from HPV infection to the development of various grades of CIN.[37-39] Furthermore, the intake of vitamin C and E may widely inhibit cervical cancer development (from HPV infection to the development of CIN 1, 2 and 3, as well as cervical cancer).[23,40-42] However, the intake of antioxidants cannot inhibit cervical cancer development without chemotherapy and radiation therapy.[26]

We suggest that the intake of antioxidants may prevent both RNA and DNA virus infection and persistent infection. However, we do not consider them to be sufficiently effective for the treatment of advanced stage disease.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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